immune response enhancers. It is urged that support for newly added claims 35-38 may be found on page 10, lines 23 - 29, page 27, lines 10-19, page 28, line 14 - page 31, line 2, and throughout the specification as originally filed.

Claims 23 and 25 have been amended to remove reference to non-elected sequences and to add the step of modulating an immune response in the patient. Claim 25 has further been amended to replace reference to sequences having 75% identity to SEQ ID NO: 33 with reference to sequences having at least 95% identity to SEQ ID NO: 33. Support for this amendment may be found on page 10, lines 23 - 29, of the specification as originally filed.

It is urged that support for all the above amendments may be found throughout the specification as originally filed and that none of the amendments constitute new matter.

The Examiner has objected to the Information Disclosure Statement filed July 12, 2001, as failing to comply with the provisions of 37 CFR §1.97, §1.98 and MPEP §609. In particular, the Examiner has objected to the information provided for sequence database accessions as being incomplete. It is the applicants' understanding that the Examiner has considered the merits of those references that he has initialed. The Examiner is respectfully requested to confirm that this is correct. A replacement Information Disclosure Statement disclosing those references not initialed by the Examiner is submitted here with, together with copies of the cited references.

Claims 25-28 stand rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure. Specifically, the Examiner has objected to the recitation of sequences having at least 75% or 90% identity to SEQ ID NO: 33.

Following the above amendments, none of the pending claims recite sequences having at least 75% or 90% identity to SEQ ID NO: 33. Amended claim 25 and newly added claim 31 are drawn to methods of modulating and enhancing, respectively, an immune response by administering compositions comprising a polypeptide, wherein the polypeptide comprises a sequence having at least 95% identity to SEQ ID NO: 33 **and has the same functional properties as SEQ ID NO: 33**. Similarly, newly added claims 35 and 37 are drawn to methods of modulating and enhancing an immune response employing compositions comprising a polypeptide, wherein the polypeptide comprises a sequence having at least 95% identity to SEQ ID NO: 33 **and is able to bind to fibroblast growth factor** (FGF).

Methods for determining the percentage identity of sequences are clearly described in the specification on page 10, line 23 - page 13, line 14. Methods for determining whether a specific polypeptide will bind to FGF are well known in the art and are exemplified by the method described in Example 5 (page 31, line 4 - page 32, line 28) of the subject specification. The preparation and use of compositions comprising the inventive polypeptides in the treatment of disorders is taught in the instant specification at page 18, line 12 - page 20, line 15. Applicants submit that one of skill in the art, on being presented with the instant specification, would reasonably expect polypeptides that have at least 95% identity to SEQ ID NO: 33 and that also possess the same functional properties as SEQ ID NO: 33 and/or an ability to bind to FGF to be effective in modulating an immune response in a patient.

It is thus urged that, on being provided with the instant specification, one of skill in the art would be able to practice the claimed methods without undue experimentation, and that the rejection of the claims under 35 USC §112, first paragraph, may be properly withdrawn.

The pending claims stand rejected under 35 USC §112, second paragraph, as being indefinite. Specifically, the Examiner has stated that claims 23-28 "are indefinite because the steps recited in the method do not necessarily achieve the goal set for the in the claim preamble". The Examiner has further objected to claims 24, 26 and 28 as reciting "the immune response is enhanced".

Claims 27 and 28 have been cancelled from the application. As noted above, independent claims 23 and 25 have been amended to include, in the body of the claim, the step of modulating an immune response in a patient, and claims 24 and 26 have been amended to independent format. It is urged that, following these amendments, one of skill in the art would clearly be able to determine the metes and bounds of the pending claims, and that the rejection of the claims under 35 USC §112, second paragraph, as being indefinite, may be properly withdrawn.

The Examiner has objected to the claims as reciting non-elected subject matter, namely SEQ ID NO: 31 and 32. As noted above, reference to these sequences has been removed from the claims.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

Early consideration and allowance of the pending claims is respectfully requested.

Early consideration and allowance of the pending claims is respectfully requested.

Respectfully submitted,

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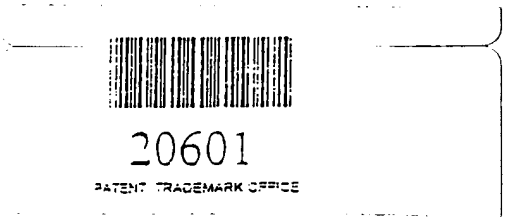
Date: June 27, 2002

SPECKMAN LAW GROUP



VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

On page 1, the first full paragraph has been replaced with the following amended paragraph:

--This application is a continuation-in-part of U.S. Patent Application No. 09/383,586, filed August 26, 1999, now U.S. Patent [6,424,419] 6,424,419; which is a continuation-in-part of U.S. Patent Application No. 09/276,268, filed March 25, 1999, now abandoned; and claims priority to International Patent Application No. PCT/NZ00/00015, filed February 18, 2000; and to U.S. Provisional Patent Application No. 60/221,216, filed July 25, 2000.--

The paragraph beginning on page 9, line 5, has been replaced with the following amended paragraph:

--The polynucleotides identified as SEQ ID NO: 1-10, 21-29, 39-46 and 58 contain open reading frames ("ORFs") or partial open reading frames encoding polypeptides or functional portions of polypeptides. Open reading frames may be identified using techniques that are well known in the art. These techniques include, for example, analysis for the location of known start and stop codons, most likely reading frame identification based on codon frequencies, etc. Open reading frames and portions of open reading frames may be identified in the polynucleotides of the present invention. Suitable tools and software for ORF analysis are available, for example, on the Internet [at http://www.ncbi.nlm.nih.gov/gorf/gorf.html]. Suitable tools and software for ORF analysis are also available through other distribution channels. Exemplary tools and software include, for example, GeneWise, available from The Sanger Center, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, United Kingdom; Diogenes, available from Computational Biology Centers, University of Minnesota, Academic Health Center, UMHG Box 43 Minneapolis MN 55455; and GRAIL, available from the Informatics Group, Oak Ridge National Laboratories, Oak Ridge, Tennessee TN. Once a partial open reading frame is identified, the polynucleotide may be extended in the area of the partial open reading frame using

techniques that are well known in the art until the polynucleotide for the full open reading frame is identified. Thus, open reading frames encoding polypeptides and/or functional portions of polypeptides may be identified using the polynucleotides of the present invention.--

The paragraph beginning on page 11, line 4, has been replaced with the following amended paragraph:

--Polynucleotide or polypeptide sequences may be aligned, and percentage of identical residues in a specified region may be determined against another polynucleotide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and FASTA algorithms. Polynucleotides may also be analyzed using the BLASTX algorithm, which compares the six-frame conceptual translation products of a nucleotide query sequence (both strands) against a protein sequence database. The similarity of polypeptide sequences may be examined using the BLASTP or FASTX algorithms. Both the BLASTN and BLASTP software are available on the NCBI anonymous FTP server [(ftp://ncbi.nlm.nih.gov) under /blast/executables/] and are available from the National Center for Biotechnology Information (NCBI), National Library of Medicine, Building 38A, Room 8N805, Bethesda, MD 20894 USA. The BLASTN algorithm versions 2.0.6 [Sept-16-1998] and version 2.0.11 [Jan-20-2000], set to the default parameters described in the documentation and distributed with the algorithm, are preferred for use in the determination of variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN and BLASTP, is described at NCBI's website [at URL http://www.ncbi.nlm.nih.gov/BLAST/newblast.html] and in the publication of Altschul *et al.*, "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", *Nucleic Acids Res.* 25:3389-3402, 1997.--

The paragraph beginning on page 11, line 24, has been replaced with the following amended paragraph:

--The computer algorithm FASTA is available on the Internet [at the ftp site ftp://ftp.virginia.edu/pub/fasta/]. The FASTA software package is also available from the University of Virginia by contacting David Hudson, Assistant Provost for Research, University

of Virginia, PO Box 9025, Charlottesville, VA 22906-9025. FASTA Version3.1t11, August 1998, set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of variants according to the present invention. The use of the FASTA algorithm is described in Pearson and Lipman, "Improved Tools for Biological Sequence Analysis," *Proc. Natl. Acad. Sci. USA* 85:2444-2448, 1988 and Pearson, "Rapid and Sensitive Sequence Comparison with FASTP and FASTA," *Methods in Enzymol.* 183:63-98, 1990. The use of the FASTX algorithm is described in Pearson *et al.*, "Comparison of DNA sequences with protein sequences," *Genomics* 46:24-36, 1997.--

Replace the paragraph beginning on page 22, line 3, with the following amended paragraph:

--In specific embodiments, the oligonucleotide probes and/or primers comprise at least about 6 contiguous residues, more preferably at least about 10 contiguous residues, and most preferably at least about 20 contiguous residues complementary to a polynucleotide sequence of the present invention. Probes and primers of the present invention may be from about 8 to 100 base pairs in length or, preferably from about 10 to 50 base pairs in length or, more preferably from about 15 to 40 base pairs in length. The probes can be easily selected using procedures well known in the art, taking into account DNA-DNA hybridization stringencies, annealing and melting temperatures, and potential for formation of loops and other factors, which are well known in the art. Tools and software suitable for designing probes, and especially suitable for designing PCR primers, are available on the Internet, for example[, at URL http://www.horizonpress.com/pcr/]. A software program suitable for designing probes, and especially for designing PCR primers, is available from Premier Biosoft International, 3786 Corina Way, Palo Alto, CA 94303-4504. Preferred techniques for designing PCR primers are also disclosed in Dieffenbach, CW and Dyksler, GS. *PCR Primer: a laboratory manual*, CSHL Press: Cold Spring Harbor, NY, 1995.--

In the Claims:

Claims 24 and 26-28 have been cancelled. The following new claims have been added:

--29. A method for enhancing an immune response in a patient, comprising:

(a) administering to the patient a composition comprising an isolated polypeptide, wherein the polypeptide comprises SEQ ID NO: 33; and

(b) enhancing an immune response in the patient.

30. The method of claim 29, wherein the composition further comprises at least one component selected from the group consisting of: physiologically acceptable carriers and non-specific immune response enhancers.

31. A method for enhancing an immune response in a patient, comprising:

(a) administering to the patient a composition comprising an isolated polypeptide, wherein the polypeptide comprises a sequence selected from the group consisting of sequences having at least 95% identity to SEQ ID NO: 33 and wherein the polypeptide has the same functional properties as SEQ ID NO: 33; and

(b) enhancing an immune response in the patient.

32. The method of claim 31, wherein the composition further comprises at least one component selected from the group consisting of: physiologically acceptable carriers and non-specific immune response enhancers.

33. The method of claim 23, wherein the composition further comprises at least one component selected from the group consisting of: physiologically acceptable carriers and non-specific immune response enhancers.

34. The method of claim 25, wherein the composition further comprises at least one component selected from the group consisting of: physiologically acceptable carriers and non-specific immune response enhancers.

35. A method for modulating an immune response in a patient, comprising:

(a) administering to the patient a composition comprising an isolated polypeptide, wherein the polypeptide comprises a sequence selected from the group consisting of sequences having at least 95% identity to SEQ ID NO: 33 and is able to bind to fibroblast growth factor; and

(b) modulating an immune response in the patient.

36. The method of claim 35, wherein the composition further comprises at least one component selected from the group consisting of: physiologically acceptable carriers and non-specific immune response enhancers.

37. A method for enhancing an immune response in a patient, comprising:

(a) administering to the patient a composition comprising an isolated polypeptide, wherein the polypeptide comprises a sequence selected from the group consisting of sequences having at least 95% identity to SEQ ID NO: 33 and is able to bind to fibroblast growth factor; and

(b) enhancing an immune response in the patient.

38. The method of claim 37, wherein the composition further comprises at least one component selected from the group consisting of: physiologically acceptable carriers and non-specific immune response enhancers.--

Claims 23 and 25 have been amended as follows:

23. (Amended) A method for modulating an immune response in a patient, comprising:

(a) administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising [an amino acid sequence selected from the group consisting of:] SEQ ID NO: [31-]33; and

(b) modulating an immune response in the patient.

25. (Amended) A method for modulating an immune response in a patient, comprising:

(a) administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence selected from the group consisting of: sequences having at least [75%] 95% identity to [a sequence of] SEQ ID NO: [31-]33, wherein the polypeptide has the same functional properties as [a sequence of] SEQ ID NO: [31-]33; and

(b) modulating an immune response in the patient.